

2. NON-TECHNICAL ABSTRACT

Malignant melanoma is a form of skin cancer that can be treated by surgical removal when it is small, but can be fatal once it has spread to other areas of the body. Melanoma will be diagnosed in over 44,000 people this year in the United States and over 7,000 people will die from this disease. Once the tumor cells have spread treatment can be difficult since the tumor usually does not respond well to chemotherapy or radiation therapy. Immunotherapy, a treatment that is designed to activate the immune response against the tumor, has shown some promise in treating advanced melanoma patients. This therapy probably works by activating T-cells in the body to find and destroy the tumor cells.

Recent studies have found that there are many different proteins produced by melanoma cells that can be seen by the T-cells. Although this may activate T-cells in some patients who have been reported to have their melanoma go away, most patients have their tumors grow without activating the T-cells. In order to fully activate the T-cells two signals must be given to them. One signal comes from these tumor proteins, called antigens. The other signal comes from a special activating protein, called a co-stimulatory molecule. One theory for why tumors are not destroyed by T-cells is that the tumor cell only has the first signal, but does not have the second signal. The most widely studied of the second signals is a protein called B7.1 and the gene for this protein has been inserted into a virus called vaccinia, which was used for prevention of smallpox throughout the world. This vaccine is being tested in melanoma patients now without significant problems. A new vaccine that contains three such molecules (B7.1, ICAM-1, and LFA-3) was made and appears much stronger in activating T-cells in the test tube.

The proposed study will use this new vaccinia virus with B7.1, ICAM-1, and LFA-3 to inject into melanoma tumors in patients with advanced disease. The goals of the study are to determine if this vaccine is safe, if the injected tumor will go away, and if the injection will cause the immune response to find other tumors and attack them as well as the injected tumor. Vaccinia virus has been given to millions of patients during the smallpox eradication program and many cancer patients have also received this virus for other types of cancer without any major side effects reported.